

Acute abdominal pain

In infancy

A. Medical causes:

1. Feeding errors:

- Underfeeding → Hunger pains.
- Overfeeding due to abdominal distension.
- Aerphagia.
- irritable mothers → they secrete catecholamine in their breast milk that pass to their infants → vomiting & abdominal pain.
- Milk allergy.

2. Urinary tract troubles:

- UTI.
- Renal stones.

3. Infections & Infestations:

- Entameba.
- Giardiasis.
- E-coli.

B. Surgical causes:

- Intussusception.
- Congenital intestinal anomalies as stenosis or malrotation.
- Visceral hernias.
- Meckel's diverticulum.

In childhood

A. Medical causes:

1. local abdominal disease:

a. Liver:

- Viral hepatitis.
- Liver abscess.
- Congestive HF.

b. Kidney:

- UTI.
- Stones.

c. Spleen:

- Congestive splenomegaly.
- Sequestration & vaso-occlusive crises in sickle cell disease.

d. Intestine:

- Heavy parasitic infestations.
- Regional enteritis.

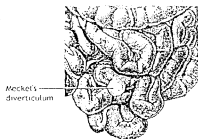
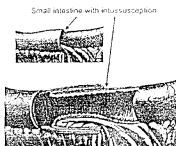
e. Lymph nodes: mesenteric adenitis & TB.

f. Pancreas: acute pancreatitis.

g. Gall bladder:

- Cholecystitis.
- Gall stones as in CHA.

h. Peritonitis.



2. General causes:

- a. DKA.
- b. Rheumatic fever.
- c. SBE.
- d. Lead poisoning.
- e. Porphyria.
- f. Hypoglycemia.

3. Referred pain from other diseases:

- a. Lower lobar pneumonia with basal pleurisy.
- b. From spine.
- c. From the pelvis: ovaries & testes.

B. Surgical causes:

1. Appendicitis.
2. Hernias (inguinal or umbilical).
3. Persistent intestinal anomalies from infancy.

Recurrent abdominal pain

A. Medical causes:1- Local abdominal disease:

1. Worm infestation: ascaris or Giardiasis
2. Chronic infection: E. coli or abdominal TB
3. Urinary tract infection or obstruction
4. Meckel's diverticulitis
5. Regional "enteritis"
6. Peptic ulcer
7. Sickle cell anemia (splenic or mesenteric infarction)
8. Gluten enteropathy with celiac crisis
9. Helicobacter pylori infection which give rise to recurrent abdominal colic's and peptic ulcers.

2- General causes:

1. Familial Mediterranean fever
2. Diabetic ketoacidosis
3. Lead poisoning
4. Porphyria
5. Visceral epilepsy
6. CNS: tumors or encephalitis.

3- Psychiatric causes:

1. School problem
2. Home problem
 - Children always present with repeated attacks of vomiting and abdominal pain in the morning (school problem) or on returning home (home problem) due to maltreatment or malbehaviour of the teachers and colleagues or due to stiff parental treatment of frustrated child.

B. Surgical causes:

1. Recurrent Intussusception
2. Recurrent hernia
3. Intra-abdominal tumor
4. Partial malrotation of the intestine.

Diagnosis

1. Careful history taking including family history.
2. Careful nutritional history as regard type of milk, amount, supplement feed, weaning, food additives ... etc
3. Thorough psychiatric history and evaluation to detect any school or home problem.
4. Meticulous and detailed history about type of pain, its character, radiation, relation to food, what increases and what relieves.
5. Thorough clinical examination of abdomen, GIT and other systems.
6. Complete urine and stool analysis.
7. Occult blood in stools.
8. Complete blood picture to detect viral and bacterial infections.
9. Blood film, hemoglobin electrophoresis to detect hemolytic anemia.
10. Tuberculin test.
11. Random blood glucose and glucose in urine with ketoses to detect diabetes.
12. X-ray for abdomen, chest, spine and urinary tract.
13. Abdominal and pelvic U/S.
14. Tests to detect typhoid fever and brucellosis.
15. Other specific tests for each disease mentioned before in the causes.

Treatment

- Is directed mainly towards the specific cause or infection according to the results of examination and investigations.

Constipation

<i>Cause</i>	<i>Example</i>
1. <u>Non-organic</u> (functional)	▪ Dietary (little water and /or fiber intake) ▪ Idiopathic
2. <u>Organic</u>	
1-Intestinal	▪ Hirschsprung disease ▪ Anal- rectal stenosis ▪ Stricture ▪ Volvulus ▪ Pseudo- obstruction
2- Drugs	▪ Narcotic ▪ Antidepressants ▪ Vincristine ▪ Antihistaminic ▪ Dehydration
3- Metabolic	▪ Cystic fibrosis (meconium ileus equivalent) ▪ Hypothyroidism ▪ Hypokalemia ▪ Hypercalcemia
4- Neuromuscular	▪ Myotonia dystrophy ▪ Spinal cord lesions (tumors, spina bifida) ▪ Amyotonia congenita ▪ Anorexia nervosa
5- Psychiatric	



Differential diagnosis of bleeding per rectum

<i>Infant</i>	<i>Child</i>	<i>Adolescent</i>
1. Dysentery 2. Bacterial enteritis 3. Milk protein allergy 4. Intussusception 5. Anal fissure	1. Dysentery. 2. Bacterial enteritis 3. Anal fissure 4. Intussusception 5. Henoch- schonlein purpura 6. colonic polyps	1. Dysentery 2. Bacterial enteritis 3. Inflammatory bowel disease 4. Colonic polyps

Differential diagnosis of hematemesis in pediatrics

Infant	Child	Adolescent
1. Reflux esophagitis 2. Stress ulcer 3. Gastritis (Helicobacter, other bacteria or drugs) 4. Bleeding disorders	1. Gastritis 2. Stress ulcer 3. Esophageal varices 4. Peptic ulcer 5. Reflux esophagitis 6. Foreign body 7. Bleeding disorders	1. Gastritis 2. Stress ulcer 3. Esophageal varices 4. Peptic ulcer

Causes of gastrointestinal obstruction

Site	Cause
Esophagus	1. <u>Congenital</u> a. esophageal atresia b. vascular rings 2. <u>Acquired</u> a. Esophageal stricture as after severe reflux. - b- Foreign body.
Stomach	1. <u>Congenital</u> a. Antral webs b. Pyloric stenosis 2. <u>Acquired</u> a. Bezoars / foreign body b. Pyloric stricture
Small intestine	1. <u>Congenital</u> 1. Duodenal atresia 2. Annular pancreas 3. Malrotation 4. Volvulus 5. Healed Atresia 6. Meconium ileus 7. Inguinal hernia 2. <u>Acquired</u> 1. Adhesions post surgery 2. Crohn's disease 3. Intussusception 4. Meconium ileus equivalent
Colon	1. <u>Congenital</u> 1. Meconium plug 2. Hirschsprung disease 3. Colonic atresia, stenosis 4. Imperforate anus 5. Rectal stenosis 6. Pseudo-obstruction 2. <u>Acquired</u> - Ulcerative colitis (toxic megacolon)

Vomiting

Definition

- It is forceful expulsion of gastric contents through the mouth.
- ❖ **Regurgitation:** is the effortless event.
- ❖ **Rumination:** is return of gastric contents to mouth + Re-chewing and reswallowing. It occurs in psychotics and mentally retarded.

Age	Causes	Features
Infant (common)	❖ Overfeeding	○ Overweight + intake more than needs
	❖ Gastroenteritis	○ V+ Diarrhea of acute Onset
	❖ Gastro-esophageal Reflux	○ Non forced vomiting
	❖ Anatomic obstruction	○ Triad of intestinal obstruction = V + constipation + abdominal distension
	❖ Systemic infection	○ Fever + symptoms of relevant infection
Child (common)	❖ Gastroenteritis	○ V+ diarrhea of acute onset.
	❖ Systemic infection	○ Signs of the underlying Disease
	❖ Toxins or drugs	○ History
	❖ Hepatitis	○ Abdominal Pain + fever. Jaundice and dark urine may appear few days later.
	❖ Peptic ulcer	○ Epigastric pain related to meals ± hematemesis
	❖ ↑intracranial pressure	○ Projectile vomiting + Headache ± neurological signs of each cause
	❖ Cyclic vomiting	○ Is usually an exclusion diagnosis
Adolescent (common)	❖ Gastroenteritis	○ V+ Diarrhea of acute onset
	❖ Systemic infection	○ As above
	❖ Toxins or drugs	○ History
	❖ Inflammatory disease bowel	○ Diffuse crampy abdominal pain ± bloody mucoid diarrhea of long duration
	❖ Appendicitis	○ Acute onset abdominal pain starting all over the abdomen then localizing to Rt. iliac fossa + tender McBurney's point
	❖ Migraine	○ Hemi cranial headache + Autonomic manifestations

❖ Bulimia	o Excess CHO intake + induced vomiting
❖ Hepatitis	o Abdominal Pain + fever. Jaundice and dark urine may appear few days later.
❖ Peptic ulcer	o Epigastric pain related to meals ± hematemesis
❖ Biliary colic	o Rt. Hypochondria colicky pain ± obstructive jaundice
❖ Renal colic	o Loin pain ± urinary symptoms
❖ Cyclic vomiting	o As above

Diarrhea

Definition

- Frequent passage (> 3 motions / day) in non breast-fed or more than normal habit in breast fed infants) of large amount of liquid stool (liquid enough to take the shape of the container).
- ❖ **Mild diarrhea** : Purging rate of 50-70 ml / kg / day
- ❖ **Moderate diarrhea** : Purging rate of 70-90 ml / kg/day
- ❖ **Severe diarrhea** : Purging rate > 90 ml / kg/day



- Frequent small volume motions following feeding may be just a result of enhanced gastro-colic reflex.
- ❖ **Dysentery = Diarrhea + tenesmus + mucus ± blood**
- Up to 7 times/D of formed stools can be considered normal in infants

Etiology

❖ Infectious:

A. Enteral Infections "1ry GE".

1. Bacterial

- o Salmonella
- o Pathogenic E-coli
- o Campylobacter
- o Staphylococcus
- o Cholera

2. Viral:

- o Rota-virus (the most common).
- o Entero-viruses "ECHO and Coxsackie"
- o Adeno-virus

3. Fungal:

- o Monilia Albicans

4. Parasitic:

- o Entameba, Giardia lamblia
- o Bilharzial

B. Toxic (complicated) GE

1. Diarrhea & vomiting are severe.
2. Fever → due to toxemia & dehydration
3. Dehydration ⇒ Why?
4. Acidosis or alkalosis.
5. Electrolyte imbalance
 - a. Hyponatremia.
 - b. Hypokalemia.
 - b. Hypocalcaemia.
 - d. Hypomagnesaemia.

Complications

1. Dehydration: The most serious complication.
2. Electrolyte imbalance (Hyponatremia, Hypernatremia & Hypokalemia are the most common).
3. Acid base disturbances (metabolic acidosis is common).
4. Malnutrition ⇒ as a result of starvation & recurrent attacks
5. Intercurrent infections.
6. Lactose intolerance
7. D.I.C.
8. Pre-renal failure & acute tubular necrosis
9. Cerebral damage Due to
 - Thrombosis
 - DIC → I.C Hge
 - Hypernatremia
10. Tetany
Due to Hypocalcaemia or Hypomagnesaemia or alkalosis during correction of acidosis
11. Iatrogenic
e.g. Fluid overload , electrolyte disturbance & acid-base disturbance
12. Immune mediated disorders
 - Reactive arthritis.
 - Guillian Barre \$.
 - Immune hemolytic anemia.
 - Glomerulonephritis.
13. Systemic effects:
 - Septicemia
 - Bacteremia.
 - Endocarditis if the infant has CHD.
 - Hemolytic Uremic \$.....see notebook of nephrology.
 - Hepatitis (amebic or pyogenic).
 - Meningitis or encephalitis (rare).

Investigations

1. Stool analysis & culture

For pus cells – RBCs , Giardia & amoeba

2. CBC

For Hct → hemoconcentration

3. Blood gases:

For acidosis or alkalosis.

4. Urine analysis & renal function**5. Serum electrolytes** Na, K, Ca and Mg**Treatment**

The main lines of treatment are :

- ❖ Prophylactic.
- ❖ ttt of the cause
- ❖ Correction of dehydration & acidosis
- ❖ Feeding
- ❖ Symptomatic

A. Prophylactic ttt:

- Encourage breast feeding.
- Delay weaning in hot weather.
- Avoid contamination.
- Vaccination against rotavirus.

B. ttt of the cause

- Trimethoprim-sulfamethoxazole combination 48 mg / kg / D orally in divided doses
- Ampicillin 50-100 mg/kg/D orally divided / 6 hrs
- Chloramphenicol
- Specific ttt for Entameba & Giardiasis : Metronidazole (flagyl)
- For campylobacter ' Erythromycin.

C. Feeding in G.E.

1. Breast feeding
 - continue on breast feeding & don't stop it
2. Artificial feeding
 - Mild G.E: continue on the same adapted formula
 - Severe G.E: lactose free milk
3. Plenty of fluids.
4. Avoid fat & increase proteins if weaned.

ttt of dehydration

2 methods for correction of dehydration

A. Oral rehydration

- This is the most important single measure in management of G.E
- Composition of oral rehydration solution (ORS)
 - o Na Cl $\Rightarrow$ 3.5 gm
 - o NaHCO₃ $\Rightarrow$ 2.5 gm
 - o KCl $\Rightarrow$ 1.5 gm
 - o Glucose $\Rightarrow$ 20 gm
- ORS is available as packets to be dissolved in 1000 ml water.
- Rehydran $\Rightarrow$ 1/5 ORS $\Rightarrow$ dissolve in 200 ml

❖ Methods of administration1) Cup or spoon

- By the mother slowly & continuously one tea spoonful / 1 min.
- Vomiting is not an indication for stopping but if vomiting is severe & persistent we usually revert to IV route

2) Dropper or syringe → may be used .3) Naso-gastric tube → if the infant is unable to ingest the ORS or refuse it❖ The amount of ORS

- The baby is given as long as he wishes guided by his thirst
- Usually the deficit is given in 4-6 hrs as follow:
 - a. In mild dehydration : 60-80 ml / kg.
 - b. In moderate dehydration : 80-100ml / kg.
 - c. In severe dehydration : 100-120ml / kg.

❖ Maintenance doses.

- a. 50 ml / one attack of vomiting .
- b. 100 ml / one attack of diarrhea.

B. I.V fluid therapyi. Initial = 20 ml / kg "1st hour" It is given for treatment of shock .

- It may be given in the form of

1. Blood
2. FFP
3. Plasma expanders
4. Ringer or ringer lactate

The aim of lactate → changed in the liver to bicarbonate → correction of acidosis.

ii. Deficit

- According to the degree of dehydration, the amount of fluid can be estimated from the following table:

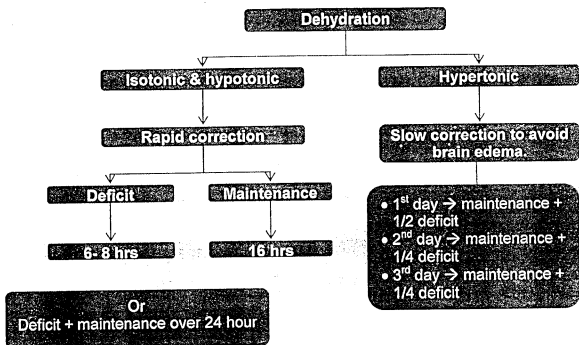
Severity	Infants (Wt < 10 kg)	Children (Wt > 10 kg)
Mild dehydration	50 ml / kg	30 ml / kg
Moderate dehydration	100 ml / kg	60 ml / kg
Severe dehydration	150 ml / kg	90 ml / kg

iii. Maintenance :

- 1st 10kgs → 100 ml / kg
- 2nd 10kgs → 50ml / kg
- >20 kgs → 20 ml / kg Or 2000 ml / m2.

Duration of correction

1. Initial ⇒ given in the 1st 1-2 hrs.
2. Deficit & maintenance depends on type of dehydration



Type of fluid

- A. Hypotonic dehydration : hypertonic solution.
 B. Hypertonic dehydration : Hypotonic solution.
 C. Isotonic dehydration : Isotonic solution.

Correction of associated electrolytes & acidosis

- 1) Hypokalemia " N. 3.5-4.5 mg/dl" → 3-5 mEq/kg
- 2) Acidosis ⇒ NaHCO₃ according to deficit in blood gases
- 3) Hypocalcaemia ⇒ Ca gluconate 10% solution slowly IV

Symptomatic ttt

1. Diarrhea:

- Anti-motility drugs : are absolutely contraindicated in GE.
- Local antiseptics can destroy the brush border of the intestine & normal bacterial flora.
- Constipating measures may impair the nutrient absorption & may lead to premature stoppage of ORT.

2. Vomiting Anti-emetics & cold drinks.

3. Abdominal distension: Potassium oral & rectal tube.

4. Colic : tincture belladonna

5. Fever: antipyretics.

Dehydration

Definition

- It is a state of -ve water balance
- It's due to *Decrease intake, Excess loss or Both

C/P

1. Acute & marked loss of body weight.
2. Depressed anterior fontanel.
3. Sunken eyes + soft intra-ocular pressure.
4. Dry tongue & mucus membrane.
5. Marked thirst.
6. Loss of skin elasticity (turgor)
7. Diminished urine flow i.e. oliguria & may be anuria.
8. Plus $\Rightarrow$ rapid & weak pulse.
9. Decrease capillary filling time
10. In severe cases $\Rightarrow$ hypotension, shock & collapse $\Rightarrow$ death.
11. Picture of complications e.g. DIC, convulsions and RF.



Degree of dehydration

According to the loss of body weight it is divided into :

A. Mild:

- Loss of up to 5% of body weight
- S&S are mild

B. Moderate :

- Loss of 5-10% of body weight
- S&S are moderate
- Manifestations of peripheral circulatory collapse may be present e.g. pallor, tachycardia & cold extremities.

C. Severe

- Loss of > 10% of body weight
- S&S are severe
- Shock & collapse are usually present

S&S	Mild	Moderate	Severe
Thirst	+	+	+++
Level of consciousness	Alert	Lethargic	Lose, even coma
Capillary refilling	2 sec.	2-4 sec.	>4 sec, cool limbs.
Mucous membranes	Normal	Dry	Very dry
Tears	Normal	Decreased	Absent
Heart rate	Normal	Increased	Markedly increased.
Respiratory rate	Normal	Increased	Rapid & deep.
BP	Normal	Normal	Decreased
Pulse	Normal	Rapid	Weak & rapid
Skin turgor	Normal	Slow	Tenting
Fontanel	Normal	Depressed	Sunken
Eyes	Normal	Sunken	Very sunken
Urine output	Normal	Oliguria	Oliguria or anuria.
	Only thirst	Thirst + signs	Thirst + signs + shock.

Types

	Hypertonic	Isotonic	Hypotonic
Incidence	5 %	80%	15%
Skin			
o Turgor	Fair(±)	Poor ++	Very poor +++
o Temperature	Hot	Cold	Cold
o Color	Gray	Gray	Gray
o Feel	Thickened	Dry	Clammy
Oral m.m	Very dry	Dry	Moist
Thirst	Severe	Mild	Absent
CNS	Convulsions	Lethargic	Coma
Serum Na	>150 mEq/L	130-150	<130 mEq/L
Osmolarity	>295 mOsm/L	275-295	<275 mOsm/L

Investigations

1. CBC : Hb & Hct values
2. Serum electrolytes Na, Ca, K
3. Blood gases
4. Renal function tests
5. ECG



N.B.: disturbance of other electrolyte may occur

Treatment

See G.E.

Electrolyte disorders

Hypokalemia

Serum K < 3.5 mEq / L

Causes

(A) ↑↑↑ Loss

1. Vomiting
2. Diarrhea
3. Fistula

(B) Regulation

1. ↑↑↑ Aldosteron:

- Conn's disease
- Cushing's.
- Steroid therapy.

2. Renal tubular defect

- Fanconi \$
- Lignac \$
- Light wood \$
- Lowe \$

3. K. Losing diuretic

Lasix

4. Cell regulation

- Alkalosis
- During management of DKA.
- β₂ agonist.

C/P

1. Arrhythmia
2. Abdominal distension & constipation.
3. Muscle Tetany

Investigations

- S.K
- Related to etiology
- ECG ⇒ low T wave, Depressed S-T segment, appearance of U-wave.

III

- Kcl = 3-5 mEq/Kg/D

Hyperkalemia

Causes

A) ↑↑↑ intake

- Toxic ingestion of K-preparations.
- IV K⁺ administration.
- Rapid infusion of old blood.

(B) Regulation

- ACE-inhibitor e.g. Captopril
- Addison disease
- Spironolactone
- CRF.

(C) Cells

- Acidosis
- DKA before tt
- Tumor lysis \$

C/P

1. Arrhythmia
2. Abdominal colic
3. Diarrhea
4. Ms weakness

Investigations

S.K > 5.5mEq / L

U/L

1. Restriction of potassium in diet
2. K- losing diuretics
3. Glucose + insulin
4. β_2 agonist inhalation
5. Dialysis

Hypernatremia

(Na⁺ > 155mEq/L)

Causes

A. ↑↑↑ intake of salts:

1. Excess salty food.
2. Ingestion of sea water.
3. Excess saline enema.
4. Hypertonic solution.
5. Excess intake of Na HCO₃ during correction of acidosis.

B. ↑↑↑ loss of water

1. Diarrhea.
2. Vomiting.
3. Excessive sweating.
4. Polyuria : DM, DI.

C. Conn's \$

Hyponatremia

Causes

1. Decrease salt in food
2. Excessive diuretics
3. Excess tap water enema
4. Hypotonic solution
5. Vomiting
6. Diarrhea
7. Psychogenic polydipsia
8. SIADH
9. Hypoaldosteronism

Acidosis

Causes

A. Metabolic

1. Diarrhea
2. CRF
3. Renal tubular defect
 - o Fanconi \$
 - o Lignac \$
 - o Light wood \$
 - o Lowe \$
4. Excess acid production
 - o DKA
 - o Tissue hypoxia

B. Respiratory

- o All causes of respiratory distress

Alkalosis

Causes

A. Metabolic:

1. Vomiting.
2. Iatrogenic due to over correction of acidosis.

B. Respiratory:

1. Hyperventilation
2. Whooping cough.

	PH	HC03	PC02
Metabolic acidosis	↓	↓	↓
Metabolic alkalosis	↑	↑	↑
Respiratory acidosis	↓	↑	↑
Respiratory alkalosis	↑	↓	↓

Viral hepatitis

Etiology

1. Hepatitis A virus
2. Hepatitis B virus
3. Non A Non B viruses
 - o Hepatitis C
 - o Hepatitis E
4. Hepatitis D: Delta hepatitis
5. Other viruses e.g. CMV, EBV, rubella, entero-viruses, HIV, Herpes viruses.

Also : Varicella, mumps, measles, may be complicated by hepatitis.

	Hepatitis A	Hepatitis B
I.P.	4-6 weeks	2-6 months
Age	Commonly in children More severe in adults	Any age
Mode of infection	• Feco-oral • Patient excrete the virus in stool 2 wks before & 1 wk after appearance of jaundice. • No Transplacental or materno-fetal infection. • No carriers	• Commonly parenteral via blood & blood products, even a prick by a contaminated needle may transmit infection. • Transplacental infection may occur • Infected mother transmit the disease to her baby during passage in birth canal

G/P

1. Fever, either low grade or high grade
2. Pain in the right hypochondrium
3. Dyspepsia
4. Jaundice
5. Tea colored urine & clay colored stool
6. Enlarged tender liver.



Complications of acute hepatitis

1. Acute fulminant hepatitis "I%"
 - more common in cases of hepatitis B when associated with delta agent → It is usually fatal
2. Post hepatitis syndrome
 - Prolonged fatigue, malaise for few months after normalization of liver function tests
 - It is usually disappear spontaneously
3. Chronic hepatitis
 - See-later
4. Cirrhosis
5. Aplastic anemia or nephrosis
6. Hepatoma

Investigations

1. Liver function tests

- SGOT (AST), SGPT (ALT) → markedly ↑↑↑
- Alkaline phosphatase & 5 nucleotidase → moderate ↑↑↑
- S. Bilirubin → ↑↑↑ both direct (early) & indirect (late).

2. Urine

- ↑↑↑ Bilirubin "direct" in the icteric stage

3. Stool: "pale".

4. Hepatitis markers

- To detect hepatitis Ags & Abs.

5. PCR

- HAV-IgM: acute infection by hepatitis A virus.
- HAV-IgG: post infection immunity to hepatitis A virus.
- HBsAg: general marker of infection by B virus.
- HBsAb: document recovery and/or immunity to HBV infection.
- Anti-HBc IgM: marker of acute infection.
- Anti-HBc IgG: past or chronic infection.
- HBeAg: indicates active replication of the virus.
- Anti-HBe: Virus no longer replicating.
- HCV ab: generally used to diagnose HCV infection.

Treatment

A. Uncomplicated cases

→ only supportive ttt

1. Bed rest
2. No restriction of certain elements of diet.
3. If severe vomiting:

- a. IV fluids to avoid dehydration.
- b. Anti-emetics are better avoided "metabolized in the liver"

4. Steroids are not indicated.

5. Interferon is tried for ttt of hepatitis-B (3 mega units 3 times / week for 6-18 months

B. Acute fulminant hepatitis

→ Manage the acute problems, while waiting for restoration of liver function.

1. Encephalopathy

→ reduce blood ammonia level by:

- a. Oral lactulose.
- b. Oral neomycin.
- c. Low protein intake

2. Bleeding:

→ fresh blood or FFP.

Chronic hepatitis

Definition

- A chronic inflammatory reaction in the liver continuing without improvement for more than 6 months

Etiology

1. Persistent viral infection

- o 15% of hepatitis-B
- o 40% of non-A non-B

2. Drugs

- o INH, sulfonamides
- o Methylidopa

3. Auto-immune "lupoid hepatitis"

4. Idiopathic

Types

According to histopathological picture it is divided into:

Chronic persistent hepatitis

1. Benign form
2. Not progressive
3. No development of cirrhosis
4. Excellent prognosis
5. Asymptomatic or non specific C/O
e.g. Anorexia, fatigue, malaise & loss of weight.
6. Vague abdominal pain & slight jaundice.
7. Liver => may be slightly enlarged & not tender.
8. Liver biopsy :
 - o Inflammatory cells are limited to portal area.
 - o Liver architecture is normal
 - o No necrosis of liver cells
 - o No evidence of fibrosis or cirrhosis
9. Laboratory findings
 - o Mild increase of SGOT (AST) & SGPT (ALT).
 - o S. albumin : Normal or slight ↑↑↑.
 - o HBs-Ag +ve in 1/3 of cases.
10. Treatment
No specific tt is needed
11. Prognosis :
Good, but persistent HBsAg carriers → ↑↑↑ risk of hepto-cellular carcinoma later in life.

B. Chronic active hepatitis

1. Symptoms are mild as chronic persistent hepatitis + fluctuating jaundice.
2. In most patients, HBs Ag is -ve "lupoid type"
3. Hepatosplenomegaly may be present in 50-80%.
4. Other organs involvement → nephritis, thyroiditis & arthritis.
5. Progress to cirrhosis or liver cell failure.

6. Liver biopsy

- o Liver architecture is distorted
- o Piece-meal necrosis & bridging i.e. necrosis between the portal tract & portal vein.
- o Cirrhosis features may be present.

7. Laboratory findings

- | | |
|---------------------|---|
| a) SGOT & SGPT | → Moderate ↑↑↑ |
| b) S. Bilirubin | → Moderate ↑↑↑ |
| c) Alk. Phosphatase | → N. or slight ↑↑↑ |
| d) S. Albumin | → ↓↓↓ |
| e) PT | → ↑↑↑ |
| f) HBs Ag | → may be +ve |
| g) Other → | - pancytopenia
- LE cells, ANA, Anti-smooth muscle Abs |

8. Treatmenta. Lupoid

- o Prednisolone 30 mg for one week 10-15 mg daily for 2-3 years.
- o Azathioprine may be given with corticosteroids 50-100mg/day.
- o Cyclosporine has been used in patients resistant to corticosteroids.

b. Viral

- o Anti-viral therapy was tried (interferon 3 meg units 3 times/week for 6-18 months).

c. Hepatic transplantation in later stages.9. Prognosis

75% respond to ttt

Nutritional liver diseases

- These are liver diseases which are caused by nutritional factors

1. KWO - Fatty infiltration

- Nutritional recovery syndrome

2. Preterm babies with high protein intake have increased morbidity & mortality3. Veno-occlusive disease4. Hemosiderosis associated with protein deficiency + increased iron intake

Veno-Occulsive disease

(Infantile liver cirrhosis)

- o Age : 1 - 4 years.
- o Sex : both sexes.

Etiology:

- There is no definite etiological hypothesis.
- It is more common in children living in rural areas with poor dietetic supply.
- Malnutrition may sensitize the human liver to the effect of toxins derived from herbs.
- Also it may be related to contamination of wheat with pyrolizidine alkaloids.
- Other toxins like aflatoxin produce similar lesions

Pathology

- Small hepatic veins as well as the central sub lobular branches are uniformly thickened described in classical V.O.D.
- Centrilobular necrosis and degeneration with fatty degeneration is present.
- Central fibrosis. follows & proceeds toward non-portal type of cirrhosis.

Clinical picture**A. Acute stage:**

1. Sudden painful hepatomegaly.
2. Ascites.
3. Jaundice is inconspicuous.
4. Recover in 6-8 weeks or patients may die of liver cell failure or pass into subacute stage.

B. Subacute stage:

Firm hepatomegaly & recurrent ascites.

- o May follow acute stage directly after a months or may appear de novo.
- o Either subsides or passes into:

C. Chronic stage

Clinically resembles other types of cirrhosis, proved by liver biopsy.

Differential diagnosis

From other causes of cirrhosis & hepatomegaly.

Management:

- Low protein & low salt diet.
- Vitamins
- Tapping of Ascites if the patient is distressed.
- Diuretics.
- Plasma & low-salt albumin in some cases.
- Steroids (tried in some cases with good results).
- Antibiotics to prevent infection.
- Omentopexy (to establish anastomosis).
- Hepatic artery ligation to decongest the liver.
- Portocaval anastomosis.

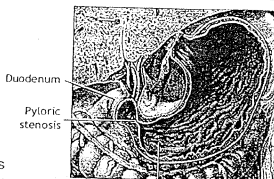
Congenital hypertrophic pyloric stenosis

Etiology

- Hypertrophy & spasm of the circular muscle of the pylorus due to unknown cause

c/p

1. Vomiting :
 - o onset:: usually between 2nd & 4th weeks
 - o character : projectile after each feeding.
2. Constipation.
3. Failure to thrive.
4. Dehydration.
5. Palpable olive green - sized mass in the Rt upper quadrant of the abdomen especially on suckling .



Pyloric part of stomach



Investigations

- Barium meal → string sign & retained gastric contents!

Treatment

- Pyloromyotomy

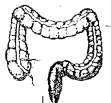
Congenital Aganglionic Megacolon

"Hirschsprung's Diseases"

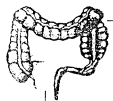
Etiology

- Absence of ganglion cells in the mucosal & muscular layers of the colon
 - o Rectum only "30%"
 - o Rectosigmoid "44%"
 - o All the colon "8%"

N.B The denervated segment is narrow ⇒ dilatation of the proximal uninvolved colon



Normal sigmoid colon and rectum



Area affected by Hirschsprung's disease

G/P

1. Constipation alternating with diarrhea "over-flow" is the commonest.
2. Abdominal distension
3. Vomiting may occur if obstruction is severe
4. Failure to thrive
5. Ribbon-like stool due to prolonged stasis in the colon .
6. Distended colon may be felt on abdominal examination
7. On rectal-examination → no feces & narrowing of aganglionic segment.

Investigations

- Barium enema → markedly dilated colon & narrowing of aganglionic segment.

INT

Colostomy then resection anastomosis

Portal hypertension

Etiology

- According to the site of obstruction of the blood flow, it is classified into :

1. Pre-sinusoidal

- A. Infra-hepatic causes :

due to obstruction of portal blood flow before entering the liver

1. Umbilical infection in the neonatal period spread through Para-umbilical v. to the portal vein → thrombosis
2. Congenital narrowing of the portal vein
3. Thrombosis of portal vein due to
 - Polycythemia
 - Dehydration
 - Peritonitis

- B. Intra-hepatic causes :

obstruction of the branches of portal vein inside the liver due to:

1. Bilharzial fibrosis
2. Infiltration by → Hodgkin's disease, leukemia & sarcoidosis

2. Sinusoidal & post-sinusoidal

- A. Intra-hepatic causes

obstruction of sinusoids & hepatic venules in the liver due to:

1. Liver cirrhosis
2. Veno-occlusive disease

- B. Supra-hepatic causes

- obstruction of the blood flow coming from the liver to Rt ventricle due to:

1. Budd-Chiari syndrome
2. High I.V.C. obstruction
3. Constrictive pericarditis & pericardial effusion.
4. R.V. failure & tricuspid regurge.



A. Symptoms

1. Gastric congestion → dyspepsia & vomiting
2. Intestinal congestion → constipation & abdominal distension
3. Hematemesis & melena → due to rupture varices
4. Abdominal enlargement → due to organomegaly

B. Signs

1. The liver:
 - a. In hepatic causes ⇒ shrunken, firm & has a sharp border.
 - b. In supra-hepatic causes ⇒ enlarged, soft & tender
 - c. In infra-hepatic causes ⇒ normal liver
2. The spleen Enlarged due to:
 - a. Portal hypertension.
 - b. RE hyperplasia
3. Ascites If portal hypertension is associated with hypo-albuminemia
4. Dilatation of the Porto-systemic anastomosis

Investigations

A. Detection of esophageal varices

1. Endoscopy
2. Barium swallow in tendlenberg position.

B. Visualization of the portal system

1. Abdominal sonar
2. CT abdomen.

C. Evaluation of the liver condition

1. Liver function tests.
2. Liver biopsy.



I. TTT of an acute attack of hematemesis:

1. Blood transfusion.
2. Vitamin K administration.
3. H2 blockers (e.g. cimetidine).
4. If the patient is cirrhotic, intestinal sterilization & measures to prevent hepatic encephalopathy (e.g. lactulose, neomycin, frequent enemas & dietary restriction of proteins).
5. Vasoactive drugs, these are used to lower portal pressure both before & as adjuvant to sclerotherapy.
6. Sungestaken-Blackemore tube.
7. Endoscopic sclerotherapy.
8. Endoscopic variceal ligation.
9. Transjugular intrahepatic Porto systemic shunt.
10. Emergency surgery if all measures failed.

II. In-between the attacks:

1. Endoscopic sclerotherapy or ligation to obliterate varices.
2. Surgical Porto systemic shunting.
3. beta adrenergic blockers: it reduce the portal pressure by splanchnic vasoconstriction & reduction of cardiac output. They also reduce hepatic arterial blood flow.

Common causes of Hepatomegaly by age group

Neonates

1. Erythroblastosis fetalis.
2. Idiopathic neonatal hepatitis.
3. Congenital infection (STORCH).
4. Prenatal and postnatal infections (viral & bacterial).
5. Congestive heart failure.
6. Biliary atresia, choledochal cyst & hemangiomas.

Infants

1. PEM.
2. Inborn errors of metabolism (CHO-lipids-proteins & pigments)
3. Cystic fibrosis.-
4. Histiocytosis.
5. Tumours:
 - o 1ry hepatoblastoma & hemangiomas.
 - o 2ry neuroblastoma & Wilm's tumor.
6. Congestive heart failure.

Children

1. PEM.
2. Toxins & drugs.
3. Parasitic infestation,
4. Tumours:
 - o 1ry Leukemia & lymphoma.
 - o 2ry neuroblastoma & Wilm's tumor.
5. Reye's syndrome.

Older children

1. Hepatitis (A,B,C&D)/
2. Chronic active hepatitis.
3. Infectious mononucleosis.
4. Wilson's disease.-
5. Drugs & toxins.
6. Tumours :1ry& 2ry.
7. Parasitic infestations as Bilharziasis.

Complications of liver cirrhosis

1. Ascites.
2. Portal hypertension.
3. Hepatic encephalopathy.
4. Hyper dynamic circulation.
5. Endocrine changes.
6. Impaired hepatic metabolism.
7. Bleeding diathesis.
8. Impaired fat absorption.
9. Susceptibility to infection.
10. Malignant Hepatoma.
11. Gall stone formation.
12. Renal failure.

Differential diagnosis of Ascites in pediatric age group

Types	Mechanism	Pathogenesis	Diagnosis
Transudate	1. Hepatic outflow obstruction	- Heart failure - Constrictive pericarditis - Budd - Chiari -	- Cardiac signs - x-ray - high ascetic protein - biopsy - urinary protein
	2. Hypoproteinemia o Increased loss o Decreased synthesis	- Nephrotic syndrome - Protein losing enteropathy - Severe malnutrition & malabsorption. - Liver failure. -	- stool Na isotope studies - wasting steatorrhoea - characteristic biopsy - splenic venogram
	3. Intrahepatic and portal obstruction with or without Hypoproteinemia	- Cirrhosis - Portal vein thrombosis (commonly neonatal sepsis)	
Exudates (high protein usually)	1. Infection	- Pyogenic , T.B - Viral e.g. :CMV in neonates	- Culture - Cell count - Ascetic tumor cells and blood
	2. Malignant disease	Wilms , neuroblastoma, carcinoma, hepatoma	- x-ray - associated pleurisy
	3. Intestinal anomalies and obstruction	in neonates e.g. malrotation.	
	4. Polyserositis		
Chylous	Obstruction to lymphatic drainage	- Trauma - Congenital anomalies - Tumor involving cisterna or thoracic duct - ? cirrhosis	- Biopsy of intestinal mucosa - Laparotomy
Biliary	spontaneous perforation of common bile duct	Unknown	Bile stained fluid
Uropathic	? urine transudation	Obstructive uropathy in neonates	

Causes of Cholestasis in Neonates and infants

Surgical

- Biliary atresia.
- Choledochal cyst.
- Cholidocholithiasis.
- Intrahepatic

Neonatal hepatitis

- Idiopathic.
- Viral: CMV, HBV, HCV, EBV, herpes, rubella.
- Bacterial: listeria, syphilis, sepsis, urinary tract infection.

Paucity of Intrahepatic bile ducts

- Syndromic (Allagile).
- Non-syndromic.
- Alpha one antitrypsin deficiency.
- Progressive familial, intrahepatic cholestasis

Metabolic causes:

- Galactosemia.
- Fructosemia.
- Tyrosinemia.
- Neimann-Pick type C.
- Gaucher disease.
- Defects in bile acid synthesis.
- Zeilweger syndrome.
- Cystic fibrosis.

Endocrine disorders

- Hypopituitarism
- Diabetes insipidus (Langerhan's cell Histeocytosis).
- Hypothyroidism
- Hypoparathyroidism.

Others

- Chromosomal anomalies: trisomies 21, 18, 13.
- Total parenteral nutrition.
- Neonatal iron storage disease.
- Inspissated bile syndrome.
- Dubin Johnson syndrome.

Hepatomegaly in infants and children

- The liver is the largest organ in the body.
- It constitutes 5% of the total body weight at birth.
- This decreases gradually till it becomes 2% in adults.
- The lower edge of the liver can be felt normally up to 3.5 cm below the right costal margin during the neonatal period. It can then be felt up to 2 cm below the right costal margin in the right mid-clavicular line till 12 years of age.

Concepts of normal liver size is based upon

The liver span of dullness to percussion i.e. percussing the upper edge (margin of dullness) at 5th intercostal space and the lower edge in right mid-clavicular line and measuring the distance in cm.

The liver span is around 4 - 4.5 cm at birth. It increases gradually till it becomes 7 cm at 3 years and 9 cm at 12 years.

Anatomical abnormalities

1. In some children the right lobe of the liver extends downwards and may be felt as a mass (Reidel's lobe).
2. The liver may be displaced downwards by diaphragm or thoracic organs giving a false impression of Hepatomegaly.
3. Situs inversus totalis: the liver is felt on the left side.



On examining the liver we should notice.

Consistency: firm, soft, hard...

Tenderness

Surface: smooth, irregular.

Border: sharp, rounded.

Masses or bruit (hemangiomas)

Pulsations (tricuspid incompetence)

Mechanisms of Hepatomegaly

1. Increase in the number or size of liver cells
1-Storage 2-Inflammation 3-Infiltration
2. Increase in size of vascular spaces
3. Increase in size of biliary spaces

I. Increase in the number or size of liver cells

1. Storage (inborn errors of metabolism)

The liver plays an important role in the metabolism of proteins, fats, carbohydrates, vitamins and minerals.

Inborn errors of metabolism of carbohydrates:

- Glucose and galactose are metabolized in the liver and the end result is the synthesis of glycogen.
- Glycogen is stored in the liver and its breakdown (glycogenolysis) is facilitated by a series of enzymes.
- Deficiency of such enzymes involved in the synthesis or degradation of glycogen causes abnormal deposition of glycogen in tissues, a condition known as glycogen storage disease.
- Galactose obtained from human breast milk lactose (glucose and galactose) is converted in the liver to glucose. Deficiency of the enzymes responsible for galactose metabolism causes abnormal accumulation of galactose metabolites in tissues, a condition known as Galactosemia.

Glycogen storage disease:

- According to enzyme deficiency more than 12 forms are known.
- According to organ involvement there are 2 forms: muscle and liver.

Clinical picture in hepatic glycogenosis:

- o Growth retardation and short stature
- o Hypoglycemia
- o Hepatomegaly
- o Some forms present with hepatosplenomegaly and portal hypertension
- o Some present with Cardiomyopathy
- o Some present with myopathy and hypotonia
- o Some present with rickets and renal enlargement

Diagnosis

- o Fasting blood glucose
- o Liver biopsy to detect the deficient enzyme

Treatment

- o Continuous supply of glucose to maintain normal blood glucose by day and during night time
- o Liver transplantation in some cases only.



Galactosemia

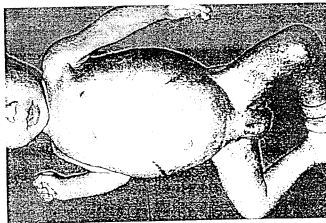
- Clinical picture
 - o Neonatal jaundice
 - o Hypoglycemia
 - o Vomiting and diarrhea
 - o Hepatosplenomegaly
 - o Cirrhosis and portal hypertension
 - o Cataract
 - o Mental retardation if not treated
- Treatment:
 - o Lactose free diet and avoid milk and its products.

Defects in lipid metabolism

- Lipidoses are inherited disorders of lipid metabolism in which abnormal amounts of lipids are stored in various tissues e.g. Gaucher disease, Neimann Pick disease..

Gaucher disease

- it is a multi system Lipidoses
- It is characterized by
 - o Hematological problems due to infiltration of the bone marrow
 - Bleeding tendency (platelet deficiency)
 - Anemia
 - Repeated infections (WBCs deficiency)
 - o Hepatosplenomegaly
 - o Skeletal and bone problems in the form of pain and fractures
 - o Neurological problems in the acute infantile neurogenic type
- It is classified into 3 types according to CNS involvement
 - o Acute infantile (neurogenic)
 - o Chronic adult (non-neurogenic)
 - o Subacute juvenile form
- Diagnosis
 - o Bone marrow aspiration and liver biopsy to detect the abnormal Gaucher cells
 - o Detection of the deficient enzyme
- Treatment
 - o Replacement of the deficient enzyme
 - o Symptomatic treatment (blood transfusion, splenectomy for hypersplenism, analgesics for bone pains)
 - o Bone marrow transplantation.



Inborn errors of proteins and amino acids metabolism

Tyrosinemia

- It is an inborn error of metabolism of the amino acid tyrosine due to deficiency of the enzymes responsible for metabolism resulting in abnormal accumulation of tyrosine and its metabolites.
- It is characterized by
 - o Neonatal Jaundice
 - o Hepatomegaly and liver cirrhosis
 - o Hemorrhage
 - o Liver cell failure in the acute severe type
 - o Renal involvement producing Fanconi syndrome and rickets
 - o Neurological involvement in the severe forms
- Diagnosis
 - o Detection of high levels of tyrosine and its metabolites in serum and urine
 - o Detection of the enzyme deficiency
- Treatment
 - o Restriction of protein and tyrosine in diet
 - o Specific drugs to prevent the formation of toxic tyrosine metabolites (NTBC)
 - o Liver transplantation.

Inborn errors of metabolism of metals and trace elements

e.g. Wilson disease, hemochromatosis

Wilson disease

- it is an inborn error of metabolism of copper resulting in abnormal accumulation of copper in the liver and other organs.
- It is characterized by
 - o Liver disease which presents in any form. It can present as acute hepatitis, acute severe fulminant hepatitis, chronic liver disease...
 - o Corneal affection in the form of gray brown ring around the cornea (Kayser Fleischer ring)
 - o Hemolysis due to affection of red blood cells.
 - o Kidney affection and renal tubular damage leading to Fanconi syndrome
 - o CNS affection (mainly basal ganglia) which appears late in the form of behavior changes, deterioration in school performance, incoordination, tremors and Dysarthria.
- Diagnosis:
 - o High urinary copper
 - o Decrease ceruloplasmin level
 - o Liver biopsy
- Treatment
 - o Copper-free diet,
 - o Copper chelating agents e.g. penicillamine.

Inborn errors of enzymes metabolism

alpha-1 antitrypsin deficiency

- It is characterized by
 - o Neonatal jaundice
 - o Hepatomegaly
 - o Bleeding tendency
 - o Liver cirrhosis and portal hypertension (splenomegaly, Ascites, bleeding esophageal varices and hematemesis)
- Diagnosis:
 - o Low serum alpha-1 antitrypsin level
 - o Protein electrophoresis
- Treatment
 - o Symptomatic e.g. sclerotherapy for esophageal varices
 - o Liver transplantation
 - o Gene therapy in the future

Other inborn errors of metabolism affecting the liver

- Mucopolysaccharidoses.
- Hepatic porphyrias.
- Hypervitaminosis A.
- Fat is stored in the liver causing hepatomegaly in obesity, diabetes mellitus, malnutrition as kwashiorkor and total parenteral alimentation.

Inflammation

A) Hepatocyte enlargement (hepatitis)

- This may be due to
 - a. Viral agents: as acute viral hepatitis A, B, C, D, E. Chronic viral hepatitis B, C, cytomegalovirus, HIV (Human Immunodeficiency Virus), Epstein-Barr virus...
 - b. Bacterial agents: as syphilis (one of STORCH), bacterial abscess, sepsis...
 - c. Parasitic and protozoal: as toxoplasmosis (one STORCH infection or intrauterine infections), Bilharziasis, Fasciola hepatica (transmitted through polluted water and vegetables irrigated with polluted water as lettuce), amoebic hepatitis and amoebic liver abscess.
 - d. Toxic agent: as drugs e.g. INH (used in treatment of T.B), paracetamol...

B) Kupffer cell enlargement:

- Kupffer cells are phagocytic cells which have an important function to remove bacterial products and antigens reaching the liver through the portal blood.
- Enlargement of Kupffer cells occurs in septicemia and infections, malignancy, granulomatous hepatitis as TB, autoimmune conditions as autoimmune hepatitis and systemic lupus.

Infiltration

- These may be:
 - a) Primary tumors as hepatoblastoma and hepatocellular carcinoma;
 - b) Secondary or metastatic as leukemia, lymphoma, neuroblastoma, Wilms tumor.

II- Increase in size of vascular spaces



- ❖ The venous blood from the liver is drained by 2 hepatic veins which drain into the inferior vena cava to the right atrium of the heart.

This increase in size of vascular spaces may be due to:

- Intrahepatic obstruction to hepatic veins outflow (veno-occlusive disease).
- Hepatic veins or high inferior vena cava obstruction e.g. by thrombosis.
- Congestive heart failure
- Constrictive pericarditis
- Hematopoietic conditions e.g. Thalassemia and sickle cell anemia.

III-Increase in size of biliary spaces

The liver has an important role in production of bile. Bile flows from the liver through bile ductules, bile ducts, common bile duct which opens in the duodenum.

The size of biliary spaces may be increased in the following conditions:

1. Extra-hepatic biliary atresia
2. Congenital hepatic fibrosis (congenital dilatation of intrahepatic bile ducts)
3. Polycystic disease of the liver
4. Choledochal cyst

Evaluation of Children with Hepatomegaly

Physical examination:

Local examination of the liver, splenomegaly, ascites

General examination we should notice

- Growth retardation: by measuring weight, height, height/weight. This growth delay and short stature is noticed in children with hepatomegaly due to
 1. Metabolic causes.
 2. Intrauterine infections.
 3. Children with liver cirrhosis.
- Face: special facial features may be noticed e.g.
 1. Mucopolysaccharidoses.
 2. Allagile syndrome.
- Eyes: They should be examined for presence of cataracts e.g. Galactosemia.
 1. Intrauterine infections.
 2. Kayser Fleischer ring in Wilson disease.
- Limbs: They should be examined to detect:
 1. Clubbing in cirrhosis.
 2. Edema in hypoalbuminemia.
 3. Rickets in tyrosinemia...
- Skin: Should be examined for presence of:
 1. Jaundice.
 2. Anemia: Which may be due to:
 - a) Bleeding from esophageal varices.
 - b) Hypersplenism.
 - c) Hemolytic anemia.
 3. Purpura: Which may be due to:
 - a) Intrauterine infections.
 - b) Hypersplenism.
 4. Skin rash.

5. Scratch marks (in cholestasis and biliary obstruction).
 6. Palmer Erythema.
 7. Spider naevi (in cirrhosis).
- Heart: Should be examined for presence of murmurs as:
 1. Pulmonary stenosis (in congenital rubella).
 2. Ventricular septal defect (in intrauterine infections).

When a child presents with hepatomegaly we should assess:

- ❖ Nature and cause of hepatomegaly.
- ❖ How to monitor response to treatment
- ❖ Severity of the condition
- ❖ Prognosis of the condition.
- ❖ If any specific treatment is required



Investigations

Baseline investigations:

- Complete blood picture
- Urine and stool analysis
- Liver function tests:
 - ❖ Synthetic:
 - Total serum proteins and serum albumin
 - Prothrombin time and partial thromboplastin time
 - ❖ Excretory:
 - Serum ALT (SGPT)
 - Serum AST (SGOT)
 - Total and direct bilirubin
 - Alkaline phosphatase
- Serum glucose and ammonia levels

Second line investigations:

- Abdominal ultrasonography
- Markers of viral hepatitis
- Serology for fascioliasis & Bilharziasis
- Bacterial culture of blood and urine
- Liver biopsy
- Study of intrauterine infections
- Investigations for metabolic diseases
- Endoscopy if needed
- Special radiological studies e.g. CT, MRI, radio isotopic scan